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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/508,897	04/28/2005	Amjad Ali	21035YP	3653

210 7590 11/24/2006

MERCK AND CO., INC
P O BOX 2000
RAHWAY, NJ 07065-0907

EXAMINER

FREISTEIN, ANDREW B

ART UNIT PAPER NUMBER

1626

DATE MAILED: 11/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/508,897

Applicant(s)

ALI ET AL.

Examiner

Andrew B. Freistein

Art Unit

1626

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION:

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 October 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-24 is/are pending in the application.
- 4a) Of the above claim(s) 22-24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-21 is/are rejected.
- 7) ☒ Claim(s) 1-21 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>1/21/05 & 9/23/2004</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-24 are currently pending.

Priority

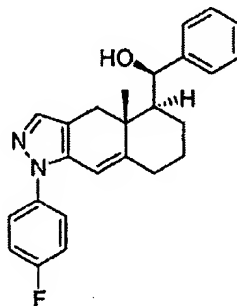
This application is a 371 of PCT/US03/10867, filed 04/08/2003, which claims benefit of U.S. Provisional Application No. 60/371,948, filed 04/11/2002.

Information Disclosure Statement

Applicant's information disclosure statements (IDS), filed on 9/23/2004 and 1/21/2005, have been considered. Please refer to Applicant's copies of the 1449 submitted herewith.

Restriction Requirement

In a response filed 10/23/2006, Applicant elected (with traverse) Group I, claims



1-21 (in part), the species of Example 35, , rheumatic disorders, and the disease rheumatoid arthritis.

Applicant traverses the restriction requirement, asserting that Examiner did not apply the unity of invention standard. However, according to MPEP 1850,

When the Markush grouping for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:

- (A) All alternatives have a common property or activity; and
- (B) (1) A common structure is present, i.e., a significant structural element is shared by all of the alternatives; or

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(B) (2) In cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

In paragraph (B)(1), above, the words "significant structural element is shared by all of the alternatives" refer to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common only a small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of existing prior art, and the common structure is essential to the common property or activity. The structural element may be a single component or a combination of individual components linked together.

In paragraph (B)(2), above, the words "recognized class of chemical compounds" mean that there is an expectation from the knowledge in the art that members of the class will behave in the same way in the context of the claimed invention. In other words, each member could be substituted one for the other, with the expectation that the same intended result would be achieved.

The fact that the alternatives of a Markush grouping can be differently classified should not, taken alone, be considered to be justification for a finding of a lack of unity of invention.

When dealing with alternatives, if it can be shown that at least one Markush alternative is not novel over the prior art, the question of unity of invention should be reconsidered by the examiner. Reconsideration does not necessarily imply that an objection of lack of unity shall be raised (emphasis added).

In the instant case, there is at least one Markush alternative that is not novel over the prior art (see US 6,831,093, cited in the restriction requirement). Consequently, the restriction is proper.

Status of the Claims

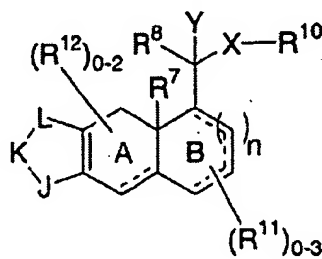
Claims 1-21 (in part) are withdrawn from further consideration by the Examiner as being drawn to non-elected inventions under 37 CFR § 1.142(b). The withdrawn subject matter is patentably distinct from the elected subject matter as it differs in

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structure and element and would require separate search considerations. In addition, a reference that anticipates one invention would not render obvious the other invention.

Elected and Examined Subject Matter

The scope of the invention of the elected subject matter and the examined subject matter is as follows:



Compounds of the Formula (I),

(R¹¹)₀₋₃, wherein:

n is 1;

J is NR¹;

K is NR³;

L is C(R⁵)(R⁶);

X, R¹, R⁸, R¹⁰ and R³ are each as defined in claim 1;

R⁵ is H, C₁₋₆alkyl, C₂₋₆alkenyl or C₃₋₆alkynyl;

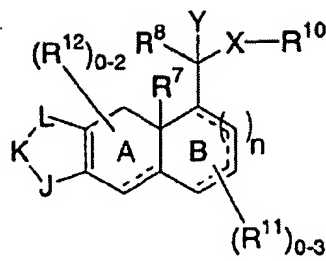
R⁶ is H, C₁₋₆alkyl, C₂₋₆alkenyl or C₃₋₆alkynyl; and

R⁷, Y, R¹¹ and R¹² are each as defined in claim 1.

Non-elected and Non-examined Subject Matter

The scope of the invention of the non-elected and non-examined subject matter is as follows:

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Compounds of the Formula (I),

 $(R^{11})_{0-3}$, wherein: n is 0 or 2; J is $C(R^1)(R^2)$; K is $C(R^3)(R^4)$; L is NR^5 ; R^2 and R^4 are each as defined in claim 1; R^5 is halo, C_{3-6} cycloalkyl, C_{1-7} alkoxy, C_{1-6} alkyl- $S(O)_k$, aryl, aralkyl, HET and C_{1-6} alkyl-HET; and R^6 is halo, C_{3-6} cycloalkyl, C_{1-7} alkoxy, C_{1-6} alkyl- $S(O)_k$, aryl, aralkyl, HET and C_{1-6} alkyl-HET.

As a result of the election and the corresponding scope of the invention, identified supra, the remaining subject matter of Claims 1-21 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to non-elected inventions. The withdrawn compounds contain varying functional groups as a result of the variables J , K , L and n , which are chemically recognized to differ in structure, function, and reactivity.

Therefore, the subject matter which was withdrawn from consideration as being non-elected subject matter materially differs in structure and composition from the elected/examined subject matter so that a reference which anticipates the

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elected/examined subject matter would not render obvious the non-elected subject matter.

Claim Rejections - 35 USC § 102

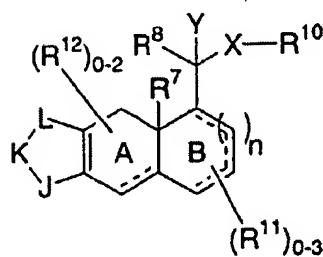
The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-21 are rejected under 35 U.S.C. 102(e) as being anticipated by Scanlan et al., US Pat. No. 6,831,093.

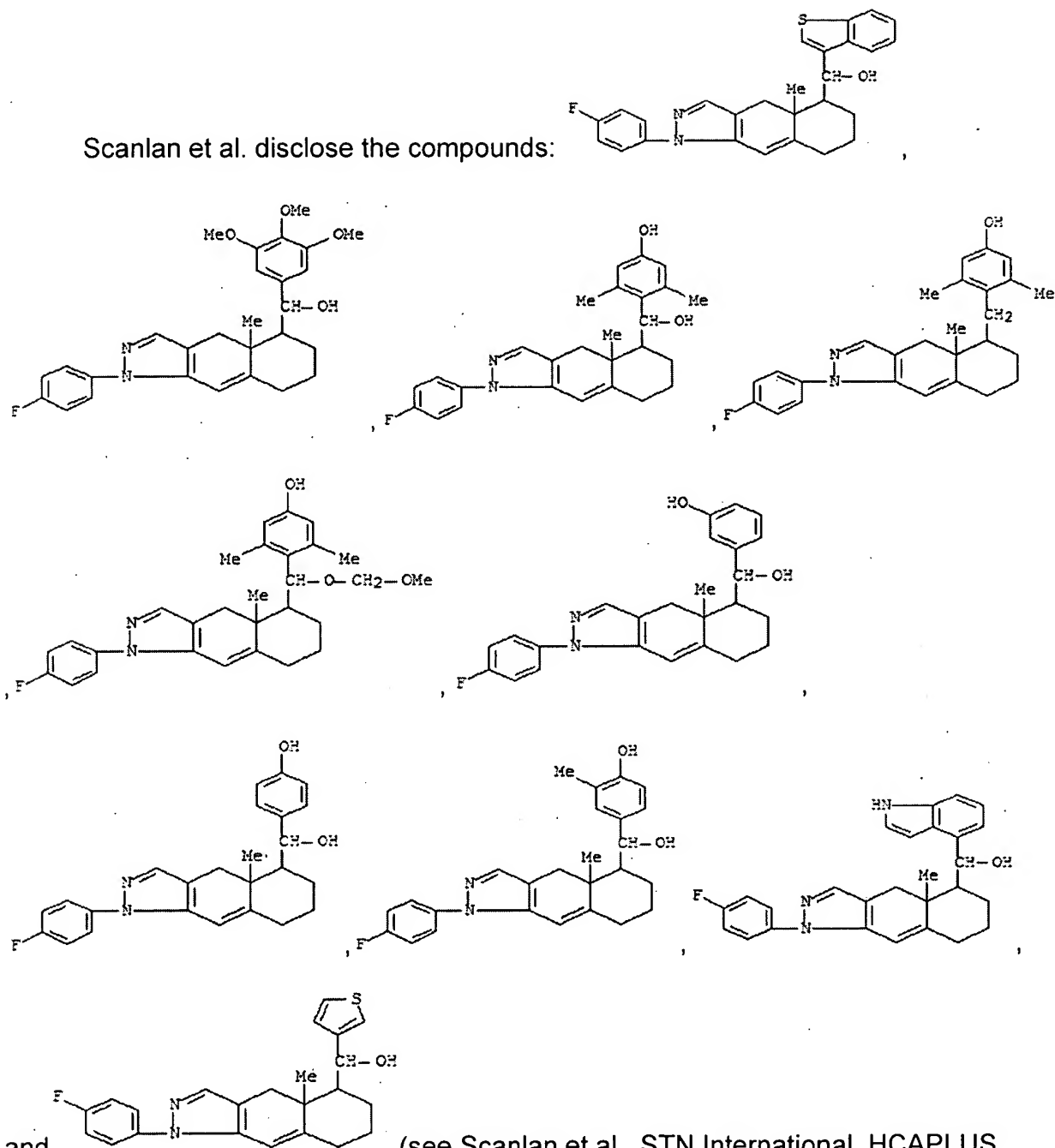
Claims 1-21 of the instant application are drawn to a compound of formula (I),



(R¹²)₀₋₂, wherein n is 1; J is NR¹; R¹ is aryl, substituted with halo; K is NR³; R³ and R⁵ create a double bond; L is C(R⁵)(R⁶); R⁶ is H; R⁷ is C₁₋₄alkyl; R⁸ is hydroxyl or C₁₋₆alkoxy; X is a bond; R¹⁰ is HET or aryl, optionally substituted with OR¹³ or C₁₋₆alkyl; R¹³ is H or C₁₋₄alkyl; Y is H; and HET is a 5- to 10-membered aromatic, partially aromatic or non-aromatic mon- or bicyclic ring, containing 1-4 heteroatoms selected from O, S, N, and optionally substituted with 1-2 oxo groups.

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Scanlan et al. disclose the compounds:



(see Scanlan et al., STN International, HCAPLUS

Database, Accession No. 2003:590999, Reg. Nos. 571202-89-6, 571202-90-9,
 57120291-0, 571202-93-2, 57120294-3, 571202-95-4, 57120296-5, 571202-97-6,
 571202-98-7 and 571202-99-8 (2006)).

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Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

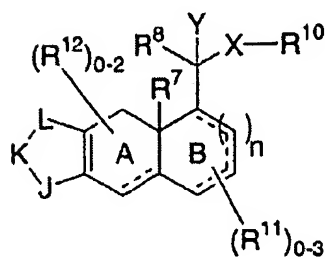
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scanlan et al., US Pat. No. 6,831,093.

Claims 1-21 of the instant application are drawn to a compound of formula (I),



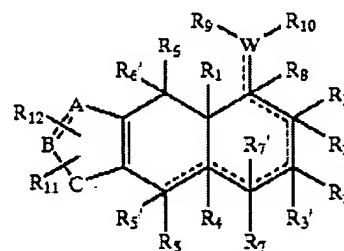
(R¹¹)₀₋₃, wherein n is 1; J is NR¹; R¹ is aryl, substituted with halo; K is NR³; R³ and R⁵ create a double bond; L is C(R⁵)(R⁶); R⁶ is H; R⁷ is C₁₋₄alkyl; R⁸ is hydroxyl or C₁₋₆alkoxy; X is a bond; R¹⁰ is HET or aryl, optionally substituted with OR¹³ or C₁₋₆alkyl; R¹³ is H or C₁₋₄alkyl; Y is H; and HET is a 5- to 10-membered aromatic,

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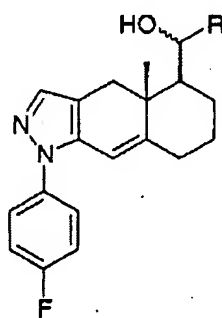
partially aromatic or non-aromatic mon- or bicyclic ring, containing 1-4 heteroatoms selected from O, S, N, and optionally substituted with 1-2 oxo groups.

The compounds claimed are selective glucocorticoid receptor modulators that have anti-inflammatory activity.

Determining the Scope and Content of the Prior Art

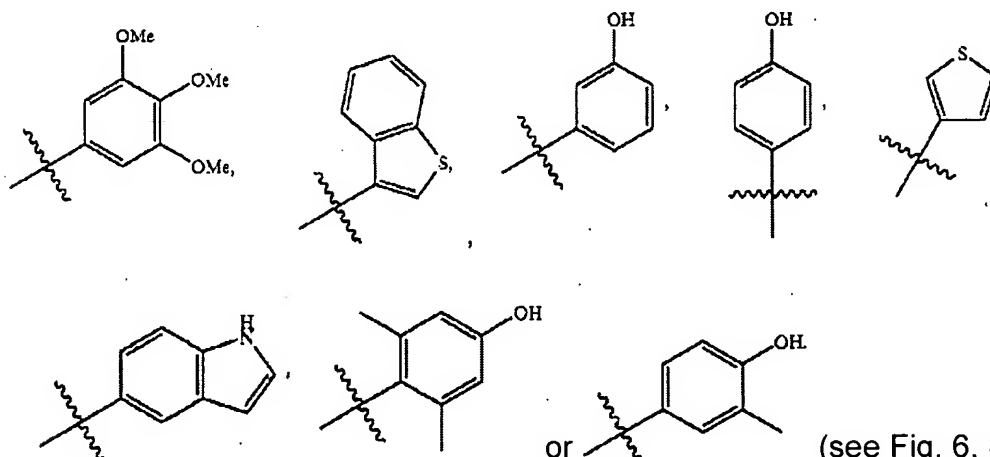


Scanlan et al. discloses compounds of the formula



more preferably, compounds of the formula 163,

, wherein R is

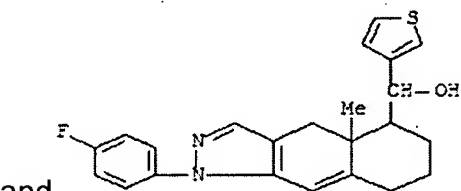
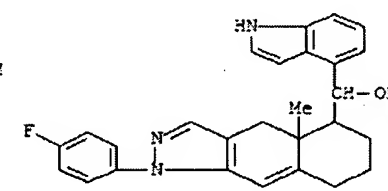
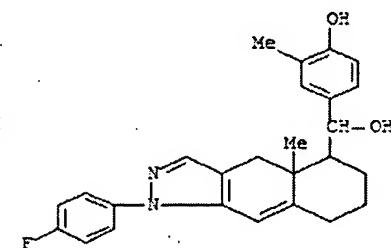
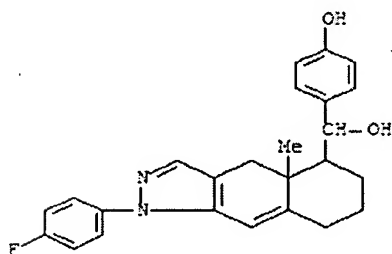
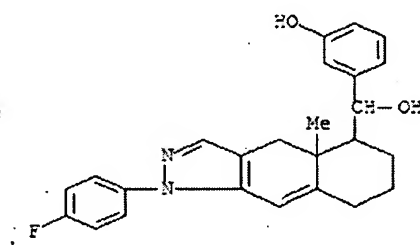
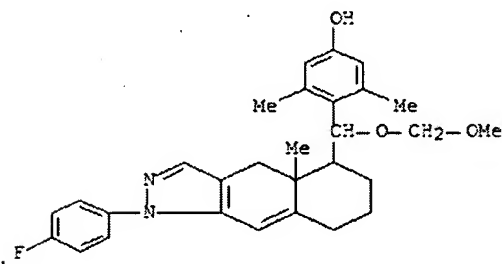
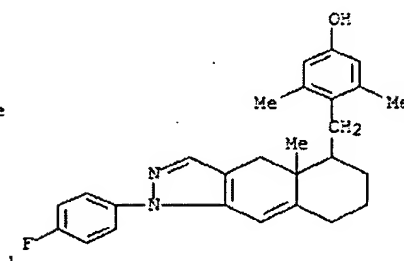
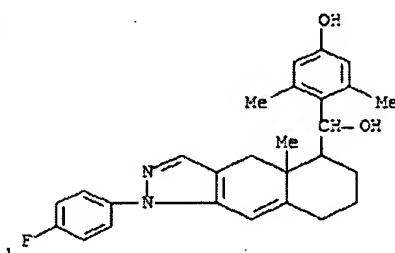
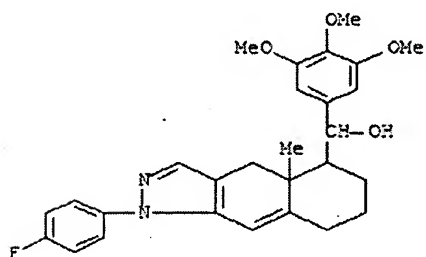
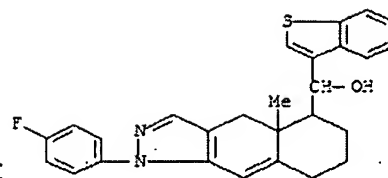


or (see Fig. 6, Scheme 6, col. 4,

lines 39-40, and col. 14, lines 12-48).

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Additionally, Scanlan et al. discloses the species:



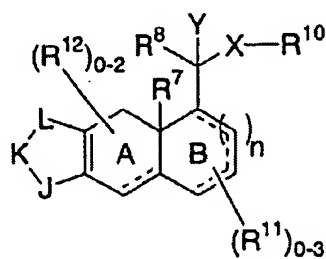
and

(see Scanlan et al., STN International, HCAPLUS

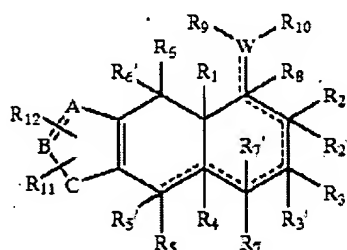
Database, Accession No. 2003:590999, Reg. Nos. 571202-89-6, 571202-90-9, 57120291-0, 571202-93-2, 57120294-3, 571202-95-4, 57120296-5, 571202-97-6, 571202-98-7 and 571202-99-8 (2006)).

The compounds disclosed are non-steroidal ligands of the glucocorticoid receptor (col. 1, lines 11-15).

Ascertaining the Differences Between the Instant Application and the Prior Art



Formula (I) of the instant application, , and formula (I) of



the prior art, , are very similar. However, the prior art

contains the variable $W(R^{10})(R^{11})$, wherein W is C, O, N or S, whereas the instant

application has the structure: bonded to ring B. Additionally, the instant application generally has only H atoms bonded to the tricyclic ring structure. On the other, hand, the prior art discloses a tricyclic structure with many variables other than H bonded to it.

Finding Prima Facie Obviousness

One of ordinary skill in the art would be motivated to produce the compounds claimed in the instant application with the prior art disclosure. Both the prior art and the instant application have the same utility and several species claimed in the instant application are specifically disclosed in the prior art. For example, Examples 39, 42,

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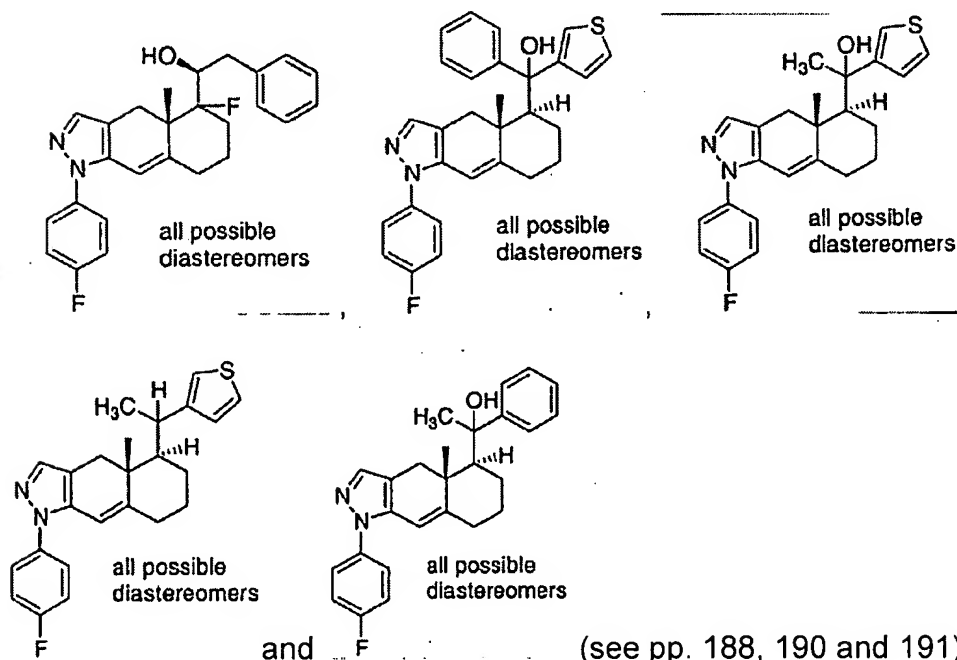
and 70 of the instant application are disclosed in the prior art. Additionally, the dependent claims in the prior art patent and the preferred embodiments in the prior art lead one of ordinary skill to prepare the instantly claimed compounds (see claim 28, scheme 6, and col. 14, lines 12-48). Therefore, the instant claims are obvious in view of the prior art.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 17 recites the limitation "all possible diastereomers" in the species:



insufficient antecedent basis for this limitation in the claim, because claim 1 is not drawn to compounds of formula (I) and all diastereomers. In order to overcome this rejection, the terms "all diastereomers" should be deleted after each species.

Claim Objections

Claims 1-21 are objected to as being drawn to non-elected subject matter.

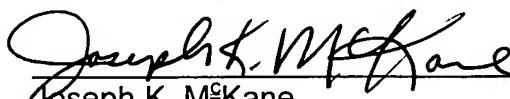
Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew B. Freistein whose telephone number is (571) 272-8515. The examiner can normally be reached Monday-Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph M^cKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

Andrew B. Freistein
Patent Examiner, AU 1626


Joseph K. M^cKane
Supervisory Patent Examiner, AU 1626
Date: November 18, 2006